THE INFLUENCE EXERTED BY NEMBUTAL ON REACTIVITY OF THE SUPERIOR COLLICULUS NEURONS

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Key words: superior colliculus, visual stimulation, Nembutal, cat

Abstract. Effects of a Nembutal upon responses of the superior colliculus neurons were analyzed in pretrigeminal cats. Most cells were studied during the spindly barbiturate pattern in the EEG. In this condition collicular neurons lose their spontaneous activity, become sluggish in their reactivity to stimuli moving at high velocity, and less sensitive to direction of movement. After a further increase in the anesthesia down to the isoelectric EEG pattern the responses of neurons were gradually depressed and finally neurons became non-driveable by visual stimulation. A possible mechanism responsible for the reduction of the cells excitability is discussed.

INTRODUCTION

In our previous study performed on the cat isolated midbrain preparation with visual input left intact, it was shown that the neurons of superior colliculus preserved their functional properties (3), whereas the amplitude of EEG simultaneously recorded from the colliculus was greatly reduced and the electric activity in the midbrain reticular formation was almost absent (13). A similar reduction of amplitude of the EEG activity can be elicited by an infusion of Nembutal in pretrigeminal cats in which an isoelectric EEG can be also achieved. It was interesting to analyze the response characteristics of single cells in a pharmacologically mediated situation. In this study functional properties of superior colliculus neurons were investigated in pretrigeminal cats during synchronized and isoelectric EEG elicited by Nembutal.
METHODS

Experiments were performed on 18 cats with pretrigeminal brain stem transection; surgery was done under ether anesthesia. Animals were paralyzed by Gallamine triethiodide (Flaxedil, 60 mg/h). Ophthalmic 0.1% atropine and 10% Neosynephrine solution were instilled into the conjunctival sacs to dilate the pupils and to retract the nictitating membranes; the animals were artificially ventilated and the CO₂ level in expired air was continuously monitored. A moving 4.5° light spot (4.5 cd/m²) and a diffuse flash (15 cd/m²) were used for stimulation. Stimuli were presented on a white concave screen with dim background illumination (0.8 cd/m²). The spot moved horizontally with one of the five following speeds: 5, 12, 30, 60 and 120°/s. Cortical EEG was recorded from the frontal area of cerebral cortex in every animal with a conventional EEG machine. In some cats parallel recordings of EEG activity in cortical and deep structures were monitored. Activity of single neurons in the superior colliculus was recorded with tungsten microelectrodes. Neural discharges were transformed into standard pulses to produce post-stimulus time histograms from which the response patterns of single neurons were analyzed. Recordings started usually 2 h after the surgery had been completed. Control recordings began before intravenous Nembutal infusion. In the next step units were tested during barbiturate spindles appearing in the EEG. This EEG pattern occurred usually after infusion of Nembutal, 5–10 mg/kg. This amount of drug was administered at a rate allowing for a stable EEG pattern during the period of time necessary for testing. In the last step neurons were analyzed during flat EEG records elicited by the increased dose of the drug. A majority of cells were, however, tested only during the barbiturate spindling in EEG records. A total of 69 neurons were investigated. From this number 18 neurons were tested before and during barbiturate spindles and two of them, which were still responsive, also during the flat EEG pattern. The speed and direction selectivity of neurons were qualified according to criteria described previously (2, 3).

RESULTS

After the infusion of the anesthetic, simultaneously with appearance of barbiturate spindles on EEG records, the background firing of collicular neurons was greatly reduced, but the visual stimulus still evoked vigorous responses in most cells (Fig. 1, 2). Of the 69 units analyzed 26 showed directional selectivity and 43 — speed selectivity. About half of the speed — selective units preferred lower velocities of the moving
spot. In this condition only about 50\% of cells tested were sensitive to diffuse flash presentation, although the latent period of responses to the onset of light (as compared to the previous control group see — (3)) remained unchanged. Responses of one cell to different velocities of the stimulus movement before and after injection of the drug are presented in Fig. 1. After Nembutal injection, as seen in this figure, the responses evoked by the spot moving with velocities of 60 and 120°/s were attenuated.

![Fig. 1. Post-stimulus time histograms of the responses of the superior collicular neuron to a spot moving with different speeds. Each column represents responses taken before (left) and after (right) Nembutal injection (10 mg/kg), respectively. Numbers between columns represent velocities of the stimulus movement. Lowering of the spot-speed was associated with lowering of the number of stimulus repetitions, started from top 128, 64, 32, 16 and 8.](image-url)
Fig. 2. Post-stimulus time (PST) histograms of the responses to spot moving with a velocity of 30°/s. Row A: PST-histogram and background EEG activity recorded before Nembutal administration. B–E: responses recorded at different times with a simultaneous increase in the level of Nembutal anesthesia from 6 to 55 mg/kg. On the right side, accompanying patterns of EEG activity recorded from the frontal cortex are shown. Sixty-four consecutive stimulus repetitions were compiled for each PST-histogram.
ated, whereas responses to velocities of 12 and 30°/s were enlarged in comparison with control records. The cell thus displayed a lower sensitivity to higher stimulus speeds and preferred the lower ones. Directional selectivity was usually reduced after infusion of the anesthetic (Fig. 2), however, sometimes slight increase of directional selectivity, especially at light level of barbiturate anesthesia, was observed (Fig. 1 — velocities 60 and 30°/s). It was very difficult to test the cells during episodes of isoelectric EEG records elicited by increased doses of Nembutal. Before the appearance of an isoelectric line EEG almost all collicular cells lost their ability of responding to visual stimulation. In 18 cats we were able to analyze only two cells displaying persistent reactions to visual stimuli during episodes of isoelectric EEG. One of these cells is presented in Fig. 2. In the absence of Nembutal, this cell had a rich background activity, and it displayed a directional selectivity in response to light spot moving with preferred speed (30°/s). During barbiturate spindles a significant reduction of spontaneous firing rate occurred but the mechanism mediating directional sensitivity was not influenced (Fig. 2B). Additional dosages of the drug (Fig. 2C, D) reduced the amplitude of EEG activity (Fig. 2D) and this reduction was followed by an arrest of the cell background firing and a disappearance of its directional sensitivity. General reactivity of the neuron to visual stimulation was still preserved irrespective of an arrest of EEG activity elicited by consecutive dose of Nembutal (Fig. 2B—E).

DISCUSSION

From the results presented above it can be seen that, during barbiturate spindles, superior collicular neurons lose their spontaneous activity. Excitability to diffuse flash is also reduced but cells still possess the ability to react to moving visual stimuli. At the same time, however, their sensitivity to higher velocity of stimulus movements is reduced and their sensitivity to direction of stimulus movement is also decreased. Similar effect elicited by Nembutal upon the spontaneous activity of neurons was found by others (1, 12). A similar influence of anesthesia on cortical visual cells such as a reduction of sensitivity to orientation, to spatial frequency and contrast was also reported (7).

Some similarities existed between present results and those obtained from experiments performed on visually deprived cats (2), on cats with ablated visual cortex (4) and with those performed on isolated midbrain preparation (3). Those similarities are expressed in a general reduction of sensitivity of superior collicular neurons to light spot moving with higher velocities and in a reduction in number of direction selective neurons. Our results show, however, that during the isoelectric-line EEG
records due to Nembutal and a similar EEG pattern characteristic for the isolated midbrain preparation (13), collicular neurons possess a different level of excitability. In the isolated midbrain preparation, in which most of the connections between the superior colliculus and other brain structures located rostrally and caudally are disrupted, with the peripheral visual input remaining intact, neurons are still excitable and have preserved most of their functional properties, whereas in nembutalized pretrigeminal preparation most cells are almost totally unresponsive (13). A general reduction in the level of sensitivity of cells elicited by Nembutal might be due to an increased postsynaptic inhibition mediated by GABA (8, 9). Iontophoretic injection of GABA to near vicinity of neurons of the retina, superior colliculus and visual cortex reduces sensitivity of these neurons with following disappearance of spontaneous firing and of discharges evoked by peripheral stimulation (5, 6, 10, 11). It was also shown, however, that Nembutal may influence responses of cells not only by an increased effectiveness of inhibition but it may also lower the level of excitation by a reduction of excitatory transmitter liberation (8).

Pronounced effects exerted by barbiturates on EEG activity are reflected on single cells as their significant lowering of reactivity to peripheral events. Effect of lowering of cells’ excitability is probably mediated by two simultaneously operating factors; an increase of inhibitory action and a reduction of effectiveness of excitatory mechanism.

We thank prof. Remigiusz Tarnecki for reading the manuscript and Mrs. Barbara Stachelska for technical assistance.

REFERENCES


Accepted 6 July 1983